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Evaluation of the relationship between gastroesophageal reflux disease and glycogenic acanthosis

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ABSTRACT

Aims: This study aims to evaluate the possible etiologic factors, espacially gastroesophageal reflux disease (GERD), in the presence of glycogenic acanthosis (GA).

Methods: A total of 387 patients who underwent upper gastrointestinal endoscopy between November 2023 and April 2024 were enrolled for the study. Participants were divided into two groups on the basis of the presence of GA. Groups were compared in terms of factors such as age, smoking, GERD, hiatal hernia, and *Helicobacter pylori*.

Results: Group comparasion revealed no significant difference except the presence of hiatus hernia, and GERD which was observed higher in the GA (+) group (p<0.001, for both parameters). In terms of the identification of the predictors of GA positivity, univariate and multiple variate analysis were performed. Only GERD (OR: 7.628, 95% CI: 3.202-18.169, p<0.001) and hiatus hernia (OR: 3.449, 95% CI: 1.387-8.579, p=0.008) were demonstrated as independent predictors of GA positivity in the multiple variate analysis.

Conclusion: In this study, we demonstrated that GA may be associated with GERD and hiatal hernia.

Keywords: Gastroesophageal reflux disease, glycogenic acanthosis, hiatal hernia

INTRODUCTION

Glycogenic acanthosis (GA) of the esophagus is a frequent incidental endoscopic observation characterized by a plaque-like appearance resulting from the accumulation of glycogen deposits in squamous epithelial cells over time.[1-3] Despite its benign nature, clinical significance and etiology of GA remains unclear.[4]

Gastroesophageal reflux disease (GERD) is a disorder which is common in the society and can occur in all age groups, characterized by regurgitation of gastric acid content into the esophagus, thay may progress with symptoms such as burning sensation and pain behind the chest, and reduces the quality of life to a certain extent.[5,6] GERD can be associated with esophagitis and hiatus hernia.[7,8] Previous studies suggest a pathophysiological link between GA and gastro-esophageal reflux.[9,10] However, there is limited consensus regarding their predictive value for GA positivity. In addition, the majority of existing studies are not up-to-date and vary in design, and limited factors that may be associated with GA have been evaluated. Therefore, the data in the literature on GA is insufficient and further studies are warranted in this field.

In the presented prospective observational study, we aimed to assess the association between the presence of GA, and GERD, and related conditions such as esophagitis and hiatus hernia.

METHODS

Ethics

This prospective observational study was conducted at Yenimahalle Training and Research Hospital and approved by Scientific Researches Assessment and Ethics Committee of the same medical institution (Date: 08.11.2023, Decision No: E-2023-59). A written informed consent was obtained from the participants for study inclusion. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Population

All consecutive eligible patients who applied to outpatient gastroenterology clinic of Yenimahalle Training and Research Hospital with dyspeptic complaints and underwent upper gastrointestinal endoscopy between November 2023 and April 2024 were involved in the study, prospectively. Subjects under 18 years of age, having previous history of gastrointestinal surgery, pregnancy, chronic diseases, anti-acid medication use, unwilling to participate in the study, suboptimal endoscopic evaluation due to patient intolerance or device-related problems, emergency endoscopy and candida esophagitis were excluded from the present research. Study participants were categorized into two separate groups and analyzed accordingly:

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those with glycogenic acanthosis (GA+ group) and those without (GA- group).

Data Collection and Definitions

Demographic data including age, sex, smoking status, history of chronic diseases and surgery, body-mass index (BMI) were collected prospectively. The GERD diagnosis was made by Gastro-esophageal Reflux Questionnaire, by evaluating the clinical reflux findings. Esophageal pH monitoring or impedance testing cannot be performed due to their unavailability. Data regarding the presence of glycogenic achantosis, hiatus hernia and esophagitis on endoscopic evaluation along with the presence of *Helicobacter pylori* (HP) on pathological examination were collected prospectively.

Detection and identification of GA was based on gastroscopic examination findings. On gastroscopy, glycogenic acanthosis manifests as multiple slightly elevated whitish plaques that are usually less than 1cm in diameter. Within the scope of the study, lesions conforming to this description have been regarded as glycogenic acanthosis, and histological confirmation has not been deemed necessary.

Esophagitis was defined as mucosal damage observed on gastro-esophageal junction during upper gastrointestinal endoscopy. Hiatal hernia was defined as the measurement of the distance greater than 3 cm between the gastroesophageal junction and the diaphragmatic hiatus during endoscopy. Diagnosis of HP infection of the gastric mucosa was performed via pathological examination.

Statistical Analysis

The normality distribution of continuous variables was analyzed by using the Kolmogorov-Smirnov test. As all continuous variables were distributed non-normally, they were given as median (interquartile range) and Mann-Whitney U test was performed for the comparison. categorical parameters were presented as frequencies (percentages) and Chi-square method was performed for analysis. Univariate binary logistic regression analyses were carried out for variables that may predict GA. After, multiple variate binary logistic regression analyses were conducted for variables that had a p-value ≤0,1 in univariate analyses. The results were presented as Odds ratio (OR), 95% confidence interval (CI), and p-value. A p-value <0,05 was considered statistically significant. IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, N.Y., USA) was used for analyses.

RESULTS

Baseline demographic data and clinical properties of the participants are presented in Table 1. The study groups does not revelaed any differences, between the GA (-) and GA (+) groups, in terms of age (median [IQR]: 58 [46.5-68.0] vs. 59.5 [53.0-66.3], p=0.341), gender distribution (female, n [%]: 178 [66.2] vs. 86 [72.9], p=0.192), smoking status (n [%]: 15 [5.6] vs. 6 [5.1], p=0.844), or BMI (median [IQR]: 25.4 [24.0-27.5] vs. 25.1 [23.9-26.7], p=0.059). Yet, significant differences were noted in the prevalence of GERD, esophagitis, and hiatus hernia (all p<0.001). Specifically, the GA (+) group showed a higher prevalence of GERD (37.3% vs. 7.1%), esophagitis (17.8% vs. 4.1%), and hiatus hernia (20.3% vs. 3.3%) compared to the GA (-) group. Detection of HP infection was observed in 129 (48.0%) and 59 (50.0%) patients in GA (-) and GA (+), respectively (p=0.711).

Table 1. Demographic, clinical characteristics and endoscopic findings of the study group

	GA (-) group (n=269)	GA (+) group (n=118)	p value
Age, years, median (IQR)	58 (46.5-68)	59.5 (53-66.25)	0.341
Gender, female, n (%)	178 (66.2)	86 (72.9)	0.192
Smoking, n (%)	15 (5.6)	6 (5.1)	0.844
BMI, kg/m², median (IQR)	25.4 (24-27.45)	25.05 (23.93-26.7)	0.059
GERD, n (%)	19 (7.1)	44 (37.3)	**<0.001**
Esophagitis present, n (%)	11 (4.1)	21 (17.8)	**<0.001**
Hiatus hernia, n (%)	9 (3.3)	24 (20.3)	**<0.001**
HP, n (%)	129 (48)	59 (50)	0.711

Significant p values are bold. GA: Glycogenic acanthosis, BMI: Body-mass index, GERD: Gastroesophageal reflux disease, HP: *Helicobacter pylori*

Table 2 presents the data of univariate and multivariate assessment for the identification of the predictors of GA positivity. In univariate analysis, BMI (OR: 0.886, 95% CI: 0.796-0.987, p=0.028), GERD (OR: 7.824, 95% CI: 4.305-14.217, p<0.001), esophagitis (OR: 5.078, 95% CI: 2.361-10.922, p<0.001), and hiatus hernia (OR: 7.376, 95% CI: 3.309-16.441, p<0.001) were revealed to be statistically significant predictors of GA positivity. However, in the multivariate analysis, only GERD (OR: 7.628, 95% CI: 3.202-18.169, p<0.001) and hiatus hernia (OR: 3.449, 95% CI: 1.387-8.579, p = 0.008) remained as independent predictors of GA positivity.

DISCUSSION

GA is an asymptomatic benign lesion of the esophagus which is often detected incidentally during endoscopic examination.[11-14] Due to its asymptomatic and benign nature, it does not require an enodoscopic follow-up program.[4] In the current literature, a definite etiology of GA has not been identified and there are insufficient studies on this subject. In previous studies, the incidence of GA was observed to increase with older age.[10,15] In the present study, no significant relationship was demonstrated between the presence of GA and age. This difference in these results can be attributed to sample size thus, multicenter studies examining the increase in the incidence of advanced age and GA are required. Smoking was also evaluated in our study and no relationship was observed in terms of GA positivity. In a previous study by Ikeda et al.[16] smoking was found to be predictor of GA presence in male subjects. In our study, smoking was not found to be a predictor of GA positivity. However, we did not evaluate the effect of smoking in gender subgroups, which may explain the different outcomes. Therefore, further studies on gender subgroups are needed to examine the association of cigarette smoking with GA, since the smoking rate is lower in the female gender subgroups. In addition, we evaluated whether HP infection is involved as a risk factor in the presence of GA. However, a significant association of HP infection with an increase in the presence of GA has not been demonstrated. Similarly, a study carried out by Emiroglu et al.[17] in a pediatric patient group showed similar results to our findings, which demonstrated no relationship between HP positivity and GA positivity. Our findings are consistent with the current literature.

Whether reflux disease has an effect on the development of GA has also been the subject of research in previous studies. Data in the literature have revealed that GERD may be involved as

Table 2. Univariate and multiple variate logistic regression analysis of predictors for GA positivity

	Univariate analysis				Multiple variate analysis			
		95% CI				95% CI		
	OR	Lower	Upper	p	OR	Lower	Upper	p
Age	1.013	0.996	1.030	0.135	-	-	-	-
Gender, male	0.728	0.451	1.174	0.193	-	-	-	-
Smoking	0.844	0.343	2.399	0.907	-	-	-	-
BMI	0.886	0.796	0.987	**0.028**	0.908	0.807	1.022	0.111
GERD	7.824	4.305	14.217	**<0.001**	7.628	3.202	18.169	**<0.001**
Esophagitis	5.078	2.361	10.922	**<0.001**	0.509	0.163	1.588	0.245
Hiatus hernia	7.376	3.309	16.441	**<0.001**	3.449	1.387	8.579	**0.008**
HP	1.085	0.704	1.673	0.711	-	-	-	-

Significant p values are bold. GA: Glycogenic acanthosis, CI: Confidence interval, BMI: Body-mass index, GERD: Gastroesophageal reflux disease, HP: *Helicobacter pylori*

a pathophysiologic factor in the process of GA development. In this concept, a researched conducted by Yılmaz et al.[10] GERD was demonstrated to be associated with GA positivity. In addition, in a study carried out by Nazlıgül et al.[15] it was similarly demonstrated that GERD and hiatal hernia were associated with the detection rate of GA. Moreover, the findings of the study by Asaoka[18] revealed a positive correlation between the GERD and GA. Consistent with the literature, our data also demonstrated a association between the GERD and GA. On the basis of these findings, it can be hypothesized that the presence of GA may be a manifestation of GERD. Therefore, clinicians may consider GERD in patients in whom GA is detected during endoscopic examination. However, prospective studies with multicenter and larger numbers of subjects are needed to support this hypothesis in order to reach a more definitive conclusion. In addition, studies examining the effect of GERD treatment on the course of GA are also warranted. Lastly, esophagitis was significantly higher in the GA (+) group, but in multivariate analyses, esophagitis could not be shown to be a predictor of GA positivity. Considering that esophagitis is not the only factor determining the severity of GERD in literature, the relationship between GERD severity and the presence of GA cannot be established based on these findings alone.[19,20] Therefore, further studies are needed to examine the relationship between the factors determining the severity of GERD and the presence of GA.

Limitations

The main limitation of our presented study is that the diagnosis of GERD cannot be confirmed by ambulatory 24h esophageal pH monitoring, since their unavailability. In addition, the long-term effects of GERD on GA could not be presented. Moreover, since the study was a single center study, it has a relatively small sample size. Lastly, histological confirmation for the diagnosis of GA could not be provided.

CONCLUSION

In conclusion, the fingings of the present study revealed an association between the presence of GA and GERD, therefore, GA may be a manifestation of GERD. Further studies are warranted on this issue.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was approved by the Scientific Researches Evaluation and Ethics Committee of Yenimahalle Training and Researches Hospital (Date: 08.11.2023, Decision No: E-2023-59).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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